MALIGNANT DISEASE OF THE LUNG WITH SPECIAL REFERENCE TO SARCOMA.[1]

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Secondary malignant disease of the lung or pleura is not uncommon. It may arise by metastasis from distant organs or by direct extension from adjacent structures. Secondary cancer of the lung may be associated with an initial focus in one of the abdominal viscera, as the liver or pancreas; but in a larger percentage of cases it results from the extension of a primary mammary, esophageal, or thyroid carcinoma. Encephaloid or medullary cancer is the form that most frequently reaches the lung by metastasis. Secondary sarcoma of the lung most commonly originates in a primary growth in the marrow cavity of one of the long bones. The small round-cell form is most often noted.

Two autonomous formations approaching closely to both carci- and sarcoma in their morphological characteristics, and appearing in many cases as secondary growths in the lungs are the so-called hypernephroma and the malignant deciduoma. Of 22 cases of hypernephroma collected from the literature by Woolley[2] there were metastasis in the lungs in 13. Although the primary growth in these cases may correspond morphologically to carcinoma or adenocarcinoma, it not rarely affords metastasis of a purely round or small spindle cell sarcomatous type. Rolleston and Marks,[3] Woolley,[4] Adami,[5] and others emphasize this point. Malignant deciduoma, which genealogically is more closely related to carcinoma than to sarcoma, involves the lungs secondarily in nearly 50 per cent. of the cases, and in some instances is first manifested by coughing, pleuritic pain, hemoptysis, and other symptoms referable to the chest.

Primary carcinoma of the lung is rare. In the records of the Breslau Pathological Institute, out of 9246 necropsies, in which there were 1000 cases of malignant disease, Pässler,[6] found 16 cases of primary carcinoma and 4 cases of primary sarcoma of the lung. Seydel[7] among 10,829 autopsies made at the Münich Pathologic Institute found records of 1342 tumors, and of these 184, or 13.7 per cent., were in the lungs or pleura. In 83.2 per cent. the tumors were metastatic and in 16.8 per cent. the tumors were primary. Of the primary growths 11 were sarcoma of the pleura and 20 were carcinoma of the lung.

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[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia), March 25, 1912.

[2] Amer. Jour. Med. Sci., cxxv, 1903.

[3] Ibid., cxvi, 1898.

[4] Loc. cit.

[5] Principles of Pathology, i, 747.

[6] Virchow's Arch., 1896, Band cxiv, S. 191.

[7] Münch. med. Woch., 1910, lvii, No. 9.

With other observers primary carcinoma has been more rare and primary sarcoma more common than the statistics indicate. Reinhard[8] found only 5 cases of primary carcinoma in 8716 necropsies. Rolleston and Trevor[9] in analyzing the post-mortem records of St. George's Hospital from January 1, 1890, to July 8, 1902, comprising 3983 cases, discovered only 8 cases of primary malignant disease of the lungs. Of these, 3 were primary sarcoma of the lung, 2 were primary sarcoma of the bronchi, and 2 were primary carcinoma of the bronchi. There was no case of primary carcinoma of the lung itself. The apparent inconsistencies in the statistics may be attributed in part to differences in nomenclature and in part also, without doubt, to the fact that some of the older writers incorrectly classified their cases. Indeed, as Mallory's[10] studies have shown, it may be very difficult or even impossible to make definite statements in regard to the cellular structure of many tumors without operative removal and immediate tissue fixation.

Primary sarcoma of the lung may spring from the lymphatic glands surrounding the bronchi, especially those in the roots of the lung, from the lymphatic vessels themselves, or from the subpleural or intrapulmonary connective tissue. Tumors developing within the lung from the connective tissue are most frequently of the spindle-cell variety, whereas those originating in the lymphatic vessels are commonly of the nature of endothelioma. Endothelioma of the pleura often invades the lung, and unless the growth is studied histologically in its entirety it may readily be mistaken for lymphosarcoma or carcinoma. As a rule, primary sarcoma is limited to one lung. It forms a large infiltrating mass, of variable consistence, and of a grayish color, often mottled with hemorrhagic areas. Metastasis, except to the mediastinal glands and tissues, are not common. In the 8 cases of primary sarcoma of the lung itself studied by Rolleston and Trevor,[11] remote metastasis were noted but once. In primary cancer, on the other hand, secondary growths are found with great frequency in the various abdominal organs, and not rarely in the muscles.[12]

The dominant symptoms of malignant disease of the lung may be those of a progressive consolidation of the lung, of stenosis of the larger bronchi or trachea, or of pleurisy with effusion. Cough and dyspnea are rarely absent. The cough varies in severity and quality, according to the size and location of the growth. It is especially marked when the larger bronchi are involved or the mediastinum is invaded and the trachea compressed. In the latter event the cough is likely to be paroxysmal and of a ringing quality, as in aneurysm of the thoracic aorta. On the other hand, when the tumor is confined almost entirely to the vesicular structure the cough may be very slight. There is also much variation in the degree of dyspnea. When the trachea is compressed, or a large pleural effusion present, it may be intense and for a considerable period the only obtrusive symptom. Expectoration occurs in a large proportion of cases, but it may be slight or even absent. Stokes laid much stress upon the occurrence of a gelatinous reddish (currant-jelly) or brownish-black (prune-juice) sputum, evidently the result of the intimate admixture of mucus and blood; but sputum of this character also occurs in other pulmonary conditions. Occasionally, disintegration of the tumor gives rise to copious fetid expectoration resembling that of gangrene. In a number of instances the diagnosis has been made certain by the microscopic examination of tissue fragments in the sputum.

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[8] Quoted by Villanene, Russkij Wratsch, October 30, 1904.

[9] Brit. Med. Jour., February 14, 1903.

[10] Jour. Med. Research, 1905, viii, 113.

[11] Loc. cit.

[12] Menetrier, Art. Neoplasie, Bouchard's Patholog. Gen., vol. ii; Handford, Trans. Path. Soc., London, 1888, xxxix, 48.

Hemoptysis, from congestion of the tissues surrounding the tumor, or erosion of fair-sized pulmonary vessels, is present in the majority of cases, and may be profuse and persistent. Pain is inconstant. It is often quite severe, however, when the pleura is involved or the thoracic nerves are compressed. Recurring attacks of pleuritic pain are not rarely the first symptom to attract attention. Enlargement of the superficial veins of the chest and localized edema sometimes result from invasion of the anterior mediastinum and occlusion of large venous trunks. More rarely, hoarseness and dysphagia arise from pressure upon the recurrent laryngeal nerve and esophagus respectively. Enlargement of the glands above the clavicle or in the arm-pit is an important symptom, but it is quite exceptional in sarcomatous cases. The temperature remains, as a rule, normal, but not infrequently in the later stages moderate fever of a remittant type supervenes and persists until the end. Cachexia sooner or later develops in most cases, and is of importance in differentiating tumor from aneurysm.

In the absence of pleural effusion, percussion usually reveals an irregular area of dulness, gradually increasing in extent. If the bronchi in the affected region are pervious, auscultation elicits bronchial breathing and broncophony. In the majority of cases, however, the bronchi are occluded, and, in consequence, both respiratory sounds and voice sounds are feeble or suppressed. When the root of the lung is involved and a main bronchus partially obstructed the respiratory sounds over a limited area may be loud and stridulous. The chest wall over the tumor is sometimes distended, but it may be retracted if there are extensive pleuritic adhesions. In tumors attaining large dimensions the heart and abdominal organs are often considerably displaced. In a case of sarcoma of the thorax cited by Rolleston[13] the liver was so depressed that its lower border was on a level with the umbilicus.

In a large percentage of cases, symptoms of pleurisy with effusion dominate the clinical picture. If the fluid is not bloody at first, it usually becomes so after two or three tappings. Microscopic examination of the sediment sometimes affords valuable diagnostic aid. A large number of cells exhibiting numerous mitoses, especially asymmetrical division forms is in favor of malignancy (Rieder, Warthin, Dock). Rarely, secondary nodules have developed along the course of the aspiration wound.

The following cases illustrate the important features of sarcoma of the lung:

CASE I.—W. P., a male, aged twenty-four years, with a good family history. His habits had been regular and he denied venereal infection. He did not recall having had any of the ordinary diseases of childhood, with the exception of diphtheria at the age of six. After that illness he enjoyed unbroken good health until about four months before admission to the hospital, January 12, when following exposure he was seized with sharp pain in the right side of the chest. His family physician treated him for pleurisy, and in four weeks his symptoms entirely disappeared. He remained in the "best of health" until six weeks before entering the hospital. At that time he developed what seemed to be a severe cold. The symptoms were those of sore throat, with hoarseness, hacking cough, and the expectoration of frothy mucus. This condition continued unchanged for about three weeks, when he noticed one morning on arising that his face was swollen, especially over the right cheek. The swelling subsided during the day, but returned each morning. Subsequently the neck and right side of the chest also became swollen. He had slight dyspnea, but no pain, and his appetite and digestion were good. On admission the patient's condition was as follows: The face, neck, and right side of the chest were markedly edematous. The skin was pale, but the appearance was not cachectic. The tongue was slightly coated, pale, and flabby. The voice was husky; beyond slight congestion of the vocal cords, however, there was nothing abnormal in the larynx. There was slight cough at intervals, with the occasional expectoration of frothy mucus. The pupils were equal and reacted well both to light and accommodation. The eye-grounds, except for slight congestion of the retinal vessels, were normal.

The right side of the chest was nearly 4 cm. larger than the left at the level of the nipples. Respiratory movements were absent on the right side and the intercostal spaces were obliterated. The apex beat was in the sixth interspace, near the anterior axillary line, and was forcible. Vocal fremitus was entirely absent over the right side, both anteriorly and posteriorly. On percussion there was flatness over the entire right side, except anteriorly above the clavicle. The cardiac dulness extended in the fifth interspace about 5 cm. to the left of the midclavicular line. On the left side there was hyperresonance. No respiratory sounds could be detected on the right side, except near the sternoclavicular articulation, where the breathing was bronchial. There were no friction sounds or rales on the right side, and vocal resonance was extremely feeble. On the left side the breath sounds were much exaggerated and scattered moist rales could be heard. A soft systolic murmur was audible at the apex of the heart, and was not transmitted. The heart sounds at the aortic area were normal. The pulmonary second sound was somewhat accentuated. The liver dulness merged above into the thoracic flatness and extended below about 5 cm. below the costal border in the midclavicular line, otherwise nothing abnormal was found in the abdomen. Neither on admission nor at any other time could enlargement of the glands in the axilla or above the clavicles be detected. The respirations were 24 to 28, and not labored; the temperature ranged between 99° and 100°; the pulses in the radial arteries were synchronous, but that on the right side was distinctly weaker than that on the left; the urine contained a trace of albumin, but no casts. Examination of the blood revealed: Hemoglobin, 65 per cent.; red blood cells, 3,872,000; white blood cells, 13,400.

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[13] Diseases of the Liver, p. 19

January 13. The right pleural cavity was tapped at two points: first, about 3 cm. below the angle of the scapula, and then 6 cm. below the angle of the scapula, near the posterior axillary line. Each puncture brought away about 50 c.c. of bloody fluid, which soon coagulated. Much resistance was offered to the entrance of the needle, and unless the direction of the cannula was frequently changed the flow of blood would cease. The clinical diagnosis was intrathoracic growth, probably sarcomatous.

January 15. The patient's condition was not materially changed.

January 16. The physical signs were unchanged. The patient stated that his appetite was good, that he had slept well, and was very comfortable. A blood examination revealed 15,600 leukocytes, of which 68.5 per cent. were polymorphonuclears, 29 per cent. were lymphocytes, 2 per cent. were large mononuclears, and 0.5 per cent. were eosinophiles.

January 17. The patient, against orders, got up and went to the toilet at the end of the ward. Returning he fell across the bed in a state of collapse, and died within a few minutes.

Autopsy. Body of a well-nourished man; skin and mucous membranes pale; rigor mortis (ten hours) well marked. Heart much displaced to left side. Left pleural sac was without adhesions and free from fluid. The left lung was somewhat congested and edematous, but otherwise normal. In the right pleural sac there were dense adhesions, with loculi containing bloody serum, the latter amounting in all to about 120 c.c. The right lung was large and firm. It weighed 2500 grams. On section it was found to be infiltrated throughout, except for a small portion of the lowest lobe posteriorly, with a dense mass of purplish gray color. A few areas of softening about the size of a pea were noted. No tuberculous foci were present. Neither the peribronchial nor the mediastinal glands were enlarged. The pericardium contained a few cubic centimeters of straw-colored fluid, and was without adhesions. The heart was slightly dilated and relaxed. It weighed 320 grams. The valves were normal. The abdominal cavity contained about 300 c.c. of clear fluid. The liver was slightly adherent to the diaphragm. It weighed 1450 grams. It was congested and apparently somewhat fatty. The spleen was congested and firm. The other abdominal organs presented no gross changes. No secondary nodules were discovered. Microscopic examination of the growth revealed a typical spindle-cell sarcoma.

Case II.—A. C., aged thirty-four years, a clerk by occupation, with a good family history. He always enjoyed good health until seven months before he came under observation, when he developed pain under his left scapula. This was shortly followed by a cough, with mucous expectoration and occasional attacks of hemoptysis. The blood was bright red in color. He sought advice in a medical dispensary and was treated for tuberculosis, but did not improve. On the contrary, his cough grew worse, his expectoration became mucopurulent and profuse, the pain continued, he developed night sweats and often felt feverish, and in three or four months lost twenty pounds.

On admission the patient weighed 118 pounds, and presented a somewhat cachectic appearance. The chest was long and flat. The left side was immobile and slightly depressed. There was no glandular enlargement. The apex beat of the heart was invisible. Tactile fremitus was marked on the right side and absent on the left side, except anteriorly above the fourth rib and posteriorly above the scapular spine. On percussion there was flatness on the left side of the chest, extending from the fifth rib anteriorly to the fourth rib in the midaxillary line, and the spine of the scapula posteriorly. Over the right lung there was hyper-resonance. On auscultation scattered dry and moist rales were heard over the right side of the chest and over the upper lobe of the left lung. On the entire right side and over the left side below the clavicle there was harsh, vesicular breathing. Over the flat area on the left side the breath sounds were scarcely audible. Examination of the heart revealed no abnormalities. The organ was apparently not displaced. The abdomen was slightly distended, but otherwise showed no changes. The temperature ranged between 97.5° F. in the morning and between 100° and 101.5° F. in the evening. The pulse was 90 to 110; the respirations were usually 24 to 30; the urine was free from albumin, casts, and sugar. An examination of the blood showed: Hemoglobin, 70 per cent.; red blood cells, 3,440,000; white blood cells, 12,400. The sputum on repeated examinations failed to show tubercle bacilli. The left pleural sac was punctured on three occasions, with negative results.

During the next four weeks there was no decided change in the general symptoms, although the patient became distinctly weaker and more emaciated. The expectoration was often blood-streaked, but only once in this period was there any marked hemoptysis. Dyspnea, which was slight at first, was now evident, especially on exertion. The fever and sweats continued as before, but there were no chills. Another examination of the blood, and the last one made, showed: Hemoglobin, 65 per cent.; red blood cells, 3,200,000; white blood cells, 14,600.

In the fifth week, during a severe paroxysm of cough, he brought up in the sputum two particles of solid matter, one about the size of a small cherry-stone, the other somewhat smaller. They were of a grayish-pink color, irregularly rounded, and firm. Upon microscopic examination these particles were found to be made up of a close aggregation of large round or slightly oval cells. The cytoplasm was abundant and the nuclei were deeply staining. There was very little interstitial reticulum. A diagnosis of intrathoracic sarcoma was now made. Three days after the expectoration of the fragments the patient was attacked with severe hemoptysis, which continued intermittently for about six hours. Following this he was much exhausted. Four days later he had another copious hemorrhage, followed by collapse, from which he never rallied. Death occurred about eight months after the appearance of the first symptom.

Autopsy. The body was much emaciated; the pleura on the left side presented firm adhesions below and posteriorly. On the right side there were slight adhesions posteriorly. Both pleural cavities contained a small quantity (50 c.c.) of bloody serum. The left leaf of the diaphragm was enormously thickened and tightly adherent to the left lung and spleen. The aorta, heart, and diaphragm were firmly united by adhesions. The bronchial, mediastinal, and abdominal glands were all much enlarged, but firm. The right lung was congested and edematous. On section the left lung, except at the apex, was found to be studded throughout with numerous pinkish-white nodules, varying in size from that of a pea to that of an egg. Most of these were firm, but two or three of the larger ones were almost gruel-like in consistence. The right lung was congested and edematous. It contained no nodules. The heart, apart from the adhesions surrounding it, showed no abnormalities. The peritoneal cavity contained no excess of fluid, but presented local adhesions in the neighborhood of the diaphragm, spleen, and left kidney. The right adrenal body was about the size of a small egg, and completely replaced by a soft, reddish-white growth. The latter also extended a short distance into the superior pole of the left kidney. The right kidney, stomach, pancreas, liver, and intestines were apparently normal. No other nodules were discovered. The brain was not examined.

Microscopically the nodules in the lung presented for the most part the same picture as the fragments found in the sputum during life, although in places the resemblance to sarcoma of the alveolar type was close.

Microscopic examination of the adrenal growth showed it to be a so-called hypernephroma, some areas presenting a typically adenocarcinomatous aspect, and others exhibiting just as definitely the characters of alveolar sarcoma.

CASE III.—G. A., a Greek, aged thirty-six years, a laborer by occupation. Owing to the lack of an efficient interpretation only an imperfect history could be obtained. He had been sick for several weeks, complaining of pain in the right side of the chest, dyspnea, and cough without expectoration. During the six days that he was under observation these symptoms were still present. He was a man of medium height, decidedly pale, but not markedly emaciated. Dyspnea was very pronounced, and his lips and finger-tips were blue. The temperature throughout was normal or subnormal; the respirations were between 24 and 36; the pulse ranged between 110 and 120; the urine was somewhat scanty, but otherwise not abnormal. An examination of the blood showed: Hemoglobin, 60 per cent., red blood cells, 3,260,000; white blood cells 12,000. The physical signs were those of a pleuritic effusion on the right side. This side of the chest was immobile and appeared to be slightly distended, although the interspaces were not obliterated. Fremitus was absent and the percussion note was flat at all points below the clavicle in front and the spine of the scapula posteriorly. The breath sounds were inaudible. Over the left side of the chest there were a few scattered coarse rales, but otherwise only the usual evidences of compensatory action. The apex beat was diffuse in the fifth interspace, and slightly to the left of the midclavicular line. There were no murmurs. The lower border of the liver could be felt below the costal margin, but apart from this the results of the abdominal examination were negative. Two punctures of the right pleural sac were made on different occasions; the first yielded a few cubic centimeters of serum faintly tinged with blood, and the second, about 80 c.c. of fluid decidedly hemorrhagic. The clinical diagnosis was pleurisy with effusion, probably tuberculous. Two days after the last aspiration pulmonary edema suddenly set in and terminated fatally.

Autopsy. At the autopsy only the thoracic findings were of interest. The right pleural cavity contained about half a liter of bloody serous fluid. The pleural surfaces were firmly adherent over the uppermost lobe, both anteriorly and posteriorly. Below there were no adhesions except over the diaphragm. The pleura throughout was enormously thickened and covered with numerous cartilaginous nodules. The right lung was compressed, hyperemic, and edematous. In the middle lobe there were two yellowish-white nodules, having a diameter of about 3 cm.; in the lowest lobe there were a number of nodules ranging in size from a millet seed to a hazelnut. The left pleural cavity was empty, and the left lung was hyperemic and edematous. The heart was pale and flabby, but otherwise not abnormal. The enlargement of the intrathoracic lymph glands could be detected.

Microscopically, sections of the pleura showed numerous anastamosing tubules lined with one or two layers of cubical epithelial cells, and separated by a rather dense network of connective tissue. Interspersing the latter were many round cells, with abundant cytoplasm, and deeply staining nuclei, somewhat like those in round-cell sarcoma. Microscopic examination of the nodules found in the lung revealed a wide-meshed net of delicate connective tissue, the meshes of which were filled with large round cells, having an epithelioid appearance. The cells were packed tightly in the acini, and were in immediate contact with the reticulum as in alveolar sarcoma. Many vessels were seen in the trabeculæ. The anatomical diagnosis was endothelioma of the right pleura with metastasis in the right lung.

The diagnosis of pulmonary malignant disease is often a matter of great difficulty, only to be arrived at by a careful collation of all the facts and a close observation of the progress of the case. Pulmonary tuberculosis, pleural effusion, or aneurysm, is usually suspected. Not rarely the symptoms throughout are so indefinite that the true nature of the condition may only be determined post mortem. The discovery of malignant disease elsewhere, of course, furnishes an important clue. This clue is likely to fail, however, when the growth is sarcoma and is primary in the lung. Even when the pulmonary affection is secondary the symptoms of the metastatic tumor may overshadow the entire clinical picture and the primary focus escape recognition, as in one of the cases cited above. Occasionally the examination of scraps of tissue found in the sputum furnishes conclusive evidence. In this way the diagnosis was established in Case II. Wolff,[14] Claisse,[15] Ehrlich,[16] Betshart,[17] Feldt,[18] Demorest[19] and Cornil[20] also cite instances in which the microscopic examination of tissue fragments from the sputum afforded decisive information. When pleural effusion is present, the character of the fluid, its rapid return after thoracentesis, and the cytological findings are sometimes suggestive. However, too much importance should not be attached to the occurrence of a slightly bloody exudate, since this is not uncommon in tuberculosis and pleurisy complicating chronic nephritis and other wasting diseases. In cases marked by consolidation of the lung, suspicion may be aroused by certain anomalies in the clinical picture, as the unusual location or distribution of the dull areas and the constant presence of blood in the sputum without tubercle bacilli. The fact must not be forgotten, however, that tuberculosis and malignant disease of the lungs not rarely coexist. Tuberculosis was present in 13 of 31 cases of malignant disease of the lung reported by Wolff[21] and in 3 of 10 cases reported by Schwalbe.[22] Hildebrand,[23] Seigert,[24] Ribbert[25] and Menetrier[26] also cite cases in which tuberculosis and malignant disease were associated in the same lung.

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[14] Fortsch. d. Med., Nos. 18 and 19, 1895.

[15] Lancet, March 11, 1899, p. 712.

[16] Quoted by Hampeln, Zeit. f. klin. Med., 1897, Band xxxii, H. 3 and 4.

[17] Virchow's Arch., Band cxliii, H. 1.

[18] Deutsch. med. Woch., 1903, xxix, No. 28.

[19] Med. Rec., January 16, 1904.

[20] Comp. rend. de Soc. Anat., January 27, 1905.

In any case much importance is to be attached to symptoms pointing to stenosis of the air passages, although in tumors developing within the lung these do not appear, as a rule, until the disease is far advanced, and even when such symptoms are well marked the existence of aneurysm must often be debated.

Pulmonary syphiloma may produce signs closely resembling tuberculosis on the one hand or malignant disease on the other. In the absence of any positive evidence of tuberculosis or malignant disease, a positive Wassermann reaction should be regarded as an indication for recourse to specific treatment. Echinococcic disease of the lung and dermoid cyst may yield most of the symptoms of malignant growth, although both are even more rare than the latter. Of 1816 cases of echinococcic disease occurring in the United States and collected by Sommer[27] the lung or pleura was involved in 147. Apart from the presence of cysts elsewhere, the expectoration of hydatid membrane, and the data afforded by thoracentesis, there are no characteristic signs. Presumptive evidence, however, might be forthcoming in the presence of pronounced eosinophilia and the fixation of complement in the hemolytic test. Exploratory puncture is not without danger, owing to the grave toxemia which may follow absorption of the hydatid fluid. Maydl[28] reports 11 cases of intrathoracic echinococcus disease in which a fatal result followed thoracentesis.

In the case of intrathoracic dermoid cyst the coughing up of hair is the only pathognomonic symptom. According to Shaw and Williams[29] this was observed in 7 of the 35 authentic cases reported in the literature up to 1905.

Except in rare cases the treatment of tumors of the lung or pleura can only be palliative. In the 31 cases analyzed by Seydel there were only 7 in which an operation would have offered the slightest chance of recovery.

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[21] Loc. cit.

[22] Deutsch. med. Woch., 1896, xii.

[23] Ziegler's Beiträge, 1888, Band ii.

[24] Virchow's Arch., 1893, Band cxxxiv.

[25] Deutsch. med. Woch., 1896, xi.

[26] Gaz. Heb. de Méd. et de Chirurg., 1899, No. 6.

[27] New York Med. Jour., August 22, 1896.

[28] Ueber Echinokokkus der Pleura, Wien, 1891.

[29] Lancet, November 4, 1905.